

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of Claims:

Claim 1 (previously presented): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a first viral vector which comprises a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is a second viral vector that does not comprise said therapeutic nucleic acid.

Claims 2 - 33 (canceled).

Claim 34 (previously presented): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is administered less than 1 hour prior to administering said viral vector.

Claim 35 (previously presented): The method according to claim 34, wherein said agent is administered less than five minutes prior to administering said viral vector.

Claim 36 (previously presented): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is administered concurrently with the viral vector.

Claim 37 (previously presented): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject a viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product and an agent that modulates Kupffer cell function in said subject, wherein said agent is a particle sufficient for phagocytosis and has a diameter of about 10 nm to about 1000 nm.

Claim 38 (previously presented): The method according to claim 1, wherein said first and/or second viral vector is an adenovirus vector.

Claim 39 (previously presented): The method according to any one of claims 34-38, wherein said viral vector is an adenovirus vector.

Claim 40 (withdrawn): The method according to claim 1, wherein said subject is a rodent.

Claim 41 (previously presented): The method according to any one of claims 1 or 34-38, wherein said subject is a primate.

Claim 42 (previously presented): The method according to claim 41, wherein said primate is a human.

Claim 43 (previously presented): The method according to claim 1, wherein said first viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial administration, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

Claim 44 (previously presented): The method according to any one of claims 34-37, wherein said viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial administration, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

Claim 45 (previously presented): The method according to any one of claims 1 and 34-37, wherein said agent is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, topical administration, intraocular administration, intrabronchial, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular delivery.

Claim 46 (previously presented): The method according to any one of claims 34-37, wherein said viral vector is a replication-defective viral vector.

Claim 47 (previously presented): A method of modulating toxicity associated with a virally encoded transgene, the method comprising administering to a subject an agent that modulates Kupffer cell level or Kupffer cell function in said subject.

Claim 48 (previously presented): The method according to claim 47, wherein said agent is administered prior to administration of a therapeutic nucleic acid encoding a therapeutic gene product.

Claim 49 (previously presented): The method according to claim 47, wherein said toxicity is hepatotoxicity.

Claim 50 (withdrawn): A method for modulating delivery of a virally encoded transgene to a subject, the method comprising:

(a) identifying a dosage inflection point of a virus containing said virally encoded transgene in said subject;

(b) comparing said inflection point to levels of a product of said virally encoded transgene in said subject; and

(c) adjusting if necessary the dose of virus administered to said subject, thereby modulating dosage of said virally encoded transgene.

Claim 51 (withdrawn): A method for modulating delivery of a virally encoded transgene to a subject, the method comprising:

(a) identifying a first dosage inflection point of a first virus not containing said encoded transgene in said subject, thereby saturating a Kupffer cell function;

(b) identifying a second dosage inflection point of a second virus containing said virally encoded transgene in said subject, wherein the dosage curve is non-linear;

(c) comparing said second inflection point to levels of a product of said virally encoded transgene in said subject; and

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(d) adjusting if necessary the doses of the first virus and second virus administered to said subject, thereby modulating dosage of said virally encoded transgene.

Claim 52 (previously presented): A pharmaceutical composition comprising a viral nucleic acid encoding a therapeutic gene product, an agent that modulates Kupffer cell function, and a pharmaceutically acceptable carrier.

Claim 53 (previously presented): The pharmaceutical composition according to claim 52, wherein said viral nucleic acid is provided in a viral particle.

Claim 54 (previously presented): The method according to claim 1, wherein said first and/or second viral vector is a replication-defective viral vector.